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(54) Title: NASAL SPRAY PRODUCTS

(57) Abstract

A nasal spray product comprising a pump-actuated nasal dispenser equipped with a reservoir, spray head and liquid/air mixing means, wherein the reservoir contains a topical nasal medicament composition in the form of a sprayable liquid comprising a carboxyl-containing polymer, a surfactant and a pharmaceutically-acceptable nasal medicament. The product provides a high availability of active ingredient and reduces the common problem of "roll-back" associated with drops and non-gellable nasal formulations.

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Nasal Spray Products

Field of the Invention

This invention relates to a nasal pharmaceutical product. In particular, it relates to a nasal pharmaceutical product in sprayable form whereby upon contact with the mucous linings of the nasal cavity the viscosity of the composition increases so as to form a gel. The composition which comprises a carboxyl-containing polymer, a surfactant and a pharmaceutically-acceptable nasal medicament has higher patient compliance, provides a high availability of active ingredient and minimizes the common problem of "roll-back" associated with drops and non-gellable nasal formulations where the liquid runs down the back of the throat or out of the front of the nose causing a nasty, medicinal aftertaste, irritation, and inaccurate dosing of the decongestant.

Background of the Invention

Various pharmaceutical preparations for application to the nasal cavity such as nasal ointments, jellies, nose drops and sprays are known in the art. Liquid nose drops and sprays have the disadvantage that it is difficult to retain the active drugs contained therein in the nasal cavity for an extended period of time and a portion of the dose often runs down the back of the throat or out of the front of the nose causing a nasty after taste, irritation of inflamed tissues and loss of drug from the nasal mucosa. In addition, they are not efficient sustained-release formulations. Nasal pharmaceutical preparations which are administrable as ointments and jellies are also unsatisfactory, however, because it is difficult to apply them to deep parts of the nasal cavity, such as the concha nasalis superior.

In the prior art attempts have been made to improve ease of administration of drugs by preparing formulations which gel on contact with viscous membranes.

WO92/00044 discloses an ophthalmic suspension or emulsion with a viscosity of from 1,000 to 30,000 mPa.s and a pH of from about 3.0 to about 6.5 containing lightly crosslinked polymers which is administrable in drop form. Upon contact of the lower pH suspension with the higher pH tear fluid of the eye, the viscosity of the suspension rapidly increases so that a gel is formed. However, nose drops are difficult to administer and therefore have low patient compliance. In addition, dosing is not always accurate when drugs are administered in drop form.

WO91/19481 discloses aqueous compositions which reversibly gel in response to simultaneous variations in at least two physical parameters such as temperature, pH or ionic strength. The compositions disclosed start with a pH in the range of from 2.5 to 6.5 and transform to visco-elastic gels when exposed to a pH of about 7.4 and a temperature of about 37°C. The compositions can be formulated to incorporate a pharmaceutical composition for utilization as droppable or injectable drug delivery systems.

Thus a need exists for compositions which are stable to long term storage, which can be administered to the nasal cavity in controlled sprayable form, and which are effective for preventing or minimizing "roll-back". A need also exists for sprayable nasal compositions having improved drug release characteristics.

Accordingly, it is an object of the present invention to provide a nasal composition in sprayable form which on contact with the mucous linings of the nasal cavity is transformed into a gel and which exhibits improved bioavailability and sustained drug release while at the same time preventing or reducing the common problem of "roll-back" associated with drops and non-gellable liquid sprays, thus preventing the nasty, medicinal aftertaste and allowing for more accurate dosing.

It is another object of the invention to provide a sprayable, gel-forming nasal composition having improved stability and spray characteristics.

Summary of the Invention

According to one aspect of the present invention there is provided a nasal spray product comprising a pump-actuated nasal dispenser equipped with a reservoir, spray head and liquid/air mixing means, wherein the reservoir contains a topical nasal medicament composition in the form of a sprayable liquid comprising:

i) from about 0.05 % to about 5 % by weight of composition of a carboxyl-containing polymer prepared by polymerizing one or more carboxyl-containing monoethyleneically unsaturated monomers and from about 0.1 % to about 5 % by weight of the polymer of a crosslinking agent,

ii) up to about 1 % by weight of composition of a surfactant selected from anionic, nonionic, cationic, amphoteric and zwitterionic surfactants and mixtures thereof, and

iii) from about 0.005 % to about 5 % by weight of composition of a pharmaceutically-acceptable nasal medicament,

wherein said composition has a low shear viscosity (measured with a Brookfield RVT Viscometer, Spindle 7, 1 r.p.m., 25°C) of from about 0 to about 300,000 mPa.s, a high shear viscosity (measured with a Brookfield RVT Viscometer, Spindle 7, 100 r.p.m., 25°C) of from about 0 to about 10,000 mPa.s and a pH in the range of from about 2.5 to about 6 and wherein the composition is administrable to the nasal cavity in sprayable form, whereby upon contact with the nasal linings of the nasal cavity the viscosity of the composition increases so as to form a viscous gel.

In another aspect of the invention there is provided the use of from about 0.05 % to about 5 % by weight of composition of a carboxyl-containing polymer in a topical nasal medicament composition for preventing or minimizing "roll-back", wherein the carboxyl-

containing polymer is prepared by polymerizing one or more carboxyl-containing monoethyleneically unsaturated monomers and from about 0.05 % to about 5 % by weight of the polymer of a crosslinking agent, and wherein the carboxyl-containing polymer is used in combination with from 0% to about 1 % by weight of a surfactant selected from anionic, nonionic, cationic, amphoteric and zwitterionic surfactants and mixtures thereof, and from about 0.005 % to about 5 % by weight of composition of a pharmaceutically-acceptable nasal medicament, and wherein the composition has a pH in the range from about 2.5 to about 6 and is administrable in sprayable form, whereby upon contact with the nasal linings of the nasal cavity the viscosity of the composition increases so as to form a viscous gel.

All levels and ratios herein are given by weight of composition unless otherwise specified.

Detailed Description of the Invention

In accordance with the first aspect of the present invention a nasal spray product is formed comprising a pump-actuated nasal dispenser equipped with a reservoir, spray head and liquid/air mixing means. The reservoir comprises a carboxyl-containing polymer, a surfactant and a nasal medicament.

The carboxyl-containing polymer is present in an amount of from about 0.05 % to about 5 %, preferably from about 0.25 % to about 2.5 % by weight of composition.

Suitable carboxyl-containing polymers for use herein are hydrophilic polymers which can be obtained by the polymerisation or copolymerisation of acrylic acid. Examples of such polymers include those commercially available under the Registered Trade Mark Carbopol (RTM) 934, 934P, 940, 941 and 974P, 980, 981 and manufactured by B.F. Goodrich Chemical Company, U.S.A. and also Noveon Polycarbophil AA-1. These polymers consist essentially of a colloidally water-soluble polyalkenyl polyether-

crosslinked polymer of acrylic acid, containing from about 0.75 % to about 2.00 % by weight of the polymer of a crosslinking agent such as for example polyalkyl sucrose or polyallyl pentaerythritol. Carbopol 934 is a water-soluble polymer of acrylic acid crosslinked with about 1 % of a polyallyl ether of sucrose having an average of about 5.8 allyl groups for each sucrose molecule. Preferred polymers for use herein have an average molecular weight in the range from about 1,000,000 to about 4,500,000. A most preferred polymer is Carbopol 974P. Although acrylic acid is the preferred carboxyl-containing monoethylenenically unsaturated monomer, other unsaturated, polymerizable carboxyl-containing monomers such as methacrylic acid, ethacrylic acid, β - methacrylic acid (crotonic acid), cis -α - methylcrotonic acid (angelic acid), trans -α - methyl - crotonic acid (tiglic acid), α - butylcrotonic acid, α - phenylacrylic acid, α - benzylacrylic acid, α - cyclohexylacrylic acid, β - phenylacrylic acid (cinnamic acid), coumaric acid (o-hydrocinnamic acid), umbellic acid (p-hydroxycoumaric acid) and the like can be used in addition to or instead of acrylic acid.

Suitable crosslinking agents for use herein include non-polyalkenyl polyether difunctional crosslinking monomers such as divinyl glycol; 2,3-dihydroxyhexa-1,5-diene; 2,5-dimethyl-1,5-hexadiene; divinylbenzene; N,N-diallylacrylamide; N,N-diallylmethacrylamide and the like. Preferred crosslinking agents are polyalkenyl polyether crosslinking agents containing two or more alkenyl ether groupings containing terminal $H_2C=C<$ groups, prepared by etherifying a polyhydric alcohol containing at least four carbon atoms and at least three hydroxyl groups with an alkenyl halide such as allyl bromide or the like, e.g. polyallyl sucrose, polyallyl pentaerythritol, or the like. Diolefinic non-hydrophilic macromeric crosslinking agents having molecular weights of from about 400 to about 8,000 such as insoluble di- and polyacrylates and methacrylates of diols and polyols, diisocyanate-hydroxyalkyl acrylate or methacrylate reaction products, and reaction products of isocyanate terminated prepolymers derived from polyester diols, polyether diols or polysiloxane diols with hydroxyalkylmethacrylates, and the like, can also be used as the crosslinking agents. The crosslinking agent is

present at a level in the range of from about 0.05 % to about 5 %, preferably from about 0.75 % to about 2 % by weight of the polymer.

A surfactant can be present in the compositions herein in an amount of up to about 1 % by weight of composition, preferably from about 0.4 % to about 0.8 % by weight, selected from anionic, nonionic, cationic, amphoteric and zwitterionic surfactants and mixtures thereof. The presence of a surfactant in the compositions herein serves to increase the stability of the composition at lower pH values. From the point of view of stability enhancement the surfactant is preferably selected from anionic, cationic, amphoteric and zwitterionic surfactants and mixtures thereof, most preferably anionic surfactants.

Suitable anionic surfactants include water-soluble salts of C_8-C_{22} alkyl benzene sulphonates, C_8-C_{22} alkyl sulphates, C_{10}-C_{18} alkyl polyethoxy ether sulphates, C_8-C_{24} paraffin sulphonates, alpha-C_{12}-24 olefin sulphonates, alpha-sulphonated C_6-C_{20} fatty acids and their esters, C_{10}-C_{18} alkyl glyceryl ether sulphonates, fatty acid monoglyceride sulphates and sulphonates, especially those prepared from coconut oil, C_8-C_{12} alkyl phenol polyethoxy ether sulphates, 2-acyloxy C_9-C_{23} alkane-1-sulphonate, and beta-alkyloxy C_8-C_{20} alkane sulphonates.

Preferably, the anionic surfactant is selected from alkali metal, alkaline earth metal, ammonium, and alkanolammonium salts of alkyl sulphates, alkyl ethoxy sulphates, alkyl benzene sulphonates and mixtures thereof.

The alkyl sulphate component is preferably a primary alkyl sulphate in which the alkyl group contains about 10-16 carbon atoms, more preferably an average of 12-14 carbon atoms. The alkyl group may be linear or branched in configuration. C_{10}-C_{16} alcohols, derived from natural fats or Ziegler olefin build-up or OXO synthesis, form suitable sources for the alkyl group. Examples of synthetically

derived materials include Dobanol 23 (RTM) sold by Shell Chemicals (UK) Ltd, Ethyl 24 sold by the Ethyl Corporation, a blend of C_{13}-C_{15} alcohols in the ratio 67% C_{13}, 33% C_{15} sold under the trade name Lutensol by BASF GmbH and Synperonic (RTM) by ICI Ltd, and Lial 125 sold by Liquichimica Italiana. Examples of naturally occurring materials from which the alcohols can be derived are coconut oil and palm kernel oil and the corresponding fatty acids.

For the purposes of the present invention any alkali metal, alkaline earth metal, ammonium or substituted ammonium cation can be used in association with the alkyl sulphate. In particular, the alkyl sulphate can be associated with a source of magnesium ions either introduced as the oxide or hydroxide to neutralise the acid, or added to the composition as a water soluble salt. A preferred alkyl sulphate surfactant for use herein is sodium lauryl sulphate.

Alkyl benzene sulphonates preferred for use in compositions of the present invention are those in which the alkyl group, which is substantially linear, contains about 10-16 carbon atoms, preferably about 11-13 carbon atoms, a material with an average chain length of 11.8 being most preferred.

The alkyl ethoxy sulphate surfactant component preferably comprises a primary alkyl ethoxy sulphate derived from the condensation products of a C_{10}-C_{16} alcohol with an average of up to 6 ethylene oxide groups. The C_{10}-C_{16} alcohol itself can be obtained from any of the sources previously described for the alkyl sulphate component. C_{12}-C_{13} alkyl ether sulphates are preferred especially those containing an average of from 1 to 3 ethylene oxide moieties per mole.

Nonionic surfactants suitable for use herein can be broadly defined as compounds containing a hydrophobic moiety and a nonionic hydrophilic moiety. Examples of the hydrophobic moiety can be alkyl, alkyl aromatic, dialkyl siloxane, and polyoxyalkylene alkyls.

Examples of hydrophilic moieties are polyoxyalkylenes, phosphine oxides, sulfoxides, amine oxides, and amides. Examples of preferred classes of nonionic organic surfactants include:

1. The polyethylene oxide condensates of alkyl phenols, e.g., the condensation products of alkyl phenols having an alkyl group containing from about 6 to about 12 carbon atoms in either a straight chain or branched chain configuration, with ethylene oxide, the said ethylene oxide being present in amounts equal to from about 1 to about 6 moles of ethylene oxide per mole of alkyl phenol. The alkyl substituent in such compounds may be derived from polymerized propylene, diisobutylene, octane or nonane, for example;
2. Those derived from the condensation of ethylene oxide with the product resulting from the reaction of propylene oxide and ethylene diamine products which may be varied in composition depending upon the balance between the hydrophobic and hydrophilic elements which is desired. For example, compounds containing from about 10% to about 40% polyoxyethylene by weight and having a molecular weight of from about 500 to about 4,000 resulting from the reaction of ethylene oxide groups with a hydrophobic base constituted of the reaction product of ethylene diamine and excess propylene oxide, said base having a molecular weight of the order of about 2,500 to about 10,000, are satisfactory;
3. The condensation product of aliphatic alcohols having from about 8 to about 20 carbon atoms, in either straight chain or branched chain configuration, with ethylene oxide, e.g., a tallow alcohol ethylene oxide condensate having from about 2 to about 10 moles of ethylene oxide per mole of tallow alcohol, the tallow alcohol fraction having from about 16 to about 18 carbon atoms.
4. Amide surfactants which include the ammonia, monoethanol, diethanol, and other alkanol amides of fatty acids having an acyl moiety of from about 8 to about 22 carbon atoms and represented by the general formula:

$$R_1\text{-}CO\text{-}N(H)_{m-1}(R_2OH)_{3-m}$$

wherein R_1 is a saturated or unsaturated, aliphatic hydrocarbon radical having from 7 to 21, preferably from 11 to 17 carbon atoms; R_2 represents a C_{1-4} alkylene group; and m is 1, 2 or 3, preferably 1. Specific examples of said amides are monoethanol coconut fatty acids amide and diethanol dodecyl fatty acid amide. These acyl moieties may be derived from naturally occurring glycerides, e.g., coconut oil, palm oil, soybean oil and tallow, but can be derived synthetically, e,g., by the oxidation of petroleum, or by hydrogenation of carbon monoxide by the Fischer-Tropsch process. The monoethanol amides and diethanolamides of C_{18-22} fatty acids are preferred.

Suitable cationic surfactants are generally quaternary ammonium compounds such as the alkylarylether dimethylbenzylammonium chlorides, for example, 2-[2-(p-octylcresoxy) ethoxy] ethyl dimethylbenzylammonium chloride. This is commercially available under the name methylbenzethonium chloride or Hyamine(RTM) 10X. The corresponding p-octylphenoxy derivative of this compound is commercially available as benzethonium chloride, and is also suitable for the present purpose, as are the alkyldimethylbenzylammonium chlorides available under the name benzalkonium chloride. Other suitable cationic surfactants include alkyltrimethylammonium chlorides of which cetyltrimethylammonium chloride is commercially available under the trade name Cetab(RTM); alkyldimethylethylammonium halides; alkylpyridinium chloride, for example, cetylpyridinium chloride; alkylimidazolinium chloride such as alkylhydroxyethylimidazolinium chloride; alkyldimethyldichlorobenzylammonium chlorides; acylcolaminoformylinethyl pyridinium chlorides available under the trade name of Emulsept(RTM); and alkylarylmethylpyridinium chlorides such as polyalkylnaphthalene methylpyridinium chloride available under the trade name Emcol(RTM). The term "alkyl" in the aforementioned anionic surfactants refers to alkyl radicals containing from eight to eighteen carbon atoms, preferably from ten to sixteen carbon atoms, and mixtures thereof, this being the range in

which quaternary ammonium compounds are considered to have good germicidal activity.

Zwitterionic surfactants can be broadly described as derivatives of aliphatic quaternary ammonium, phosphonium, and sulfonium compounds, in which the aliphatic radical may be straight chain or branched, and wherein one of the aliphatic substituents contains from about 8 to about 18 carbon atoms and one contains an anionic water solubilizing group, e.g. carboxy, sulfo, sulfato, phosphato, or phosphono. Examples of compounds falling within this definition are 3-(N,N-dimethyl-N-hexadecylammonio) propane-1-sulfonate and 3-(N,N-dimethyl-N-hexadecylammonio)-2-hydroxy propane-1-sulfonate.

Amphoteric surfactants can be broadly described as derivatives of aliphatic secondary and tertiary amines, in which the aliphatic radical may be straight chain or branched and wherein one of the aliphatic substituents contains from about 8 to 18 carbon atoms and one contains an anionic water solubilizing group, e.g., carboxy, sulfo, sulfato, phosphato, or phosphono. Examples of compounds falling within this definition are sodium-3-dodecylaminopropionate and sodium-3-dodecylaminopropane sulfonate.

There is also present herein a pharmaceutically-acceptable nasal medicament, i.e. a drug suitable for application via the nasal cavity, in an amount in the range of from about 0.005 % to about 5 %, preferably from about 0.01 % to about 2 % by weight of composition. Drugs suitable for use in the compositions herein can be selected appropriately according to the disease to which the composition is to be applied. In the present invention the drug is preferably an agent for treating or preventing a nasal or upper respiratory disease, preferably a vasoconstrictor or other nasal decongestant. Furthermore the drug should not react with either the carboxyl-containing polymer or the anionic surfactant. Suitable drugs may be in solid or liquid form, preferably liquid form.

Examples of such drugs include antipyretic and analgesic agents, antiphlogistics, antiarrhythmics, hypotensors, vasodilators, anticholinergics, antiarteriosclerotics, agents for circulatory systems, antitussives, expectorants, ulcer preventives, enzyme preparations, anti-malignants, chemotherapeutic agents, antihistamine agents, enzyme preparations, local anaesthetic agents, steroidal anti-inflammatory agents, non-steroidal anti-inflammatory agents, anti-allergic agents, vasoconstrictors, and mixtures thereof.

In compositions to be used for treating or preventing nasal or upper respiratory diseases, drugs effective for treatment or prevention of nasal diseases, such as anti-inflammatory agents, antihistamine agents, anticholinergics, anti-allergic agents or vasoconstrictors, are preferred. A highly preferred drug for inclusion in the composition of the present invention is a vasoconstrictor.

Suitable vasoconstrictors for use herein include phenylephrine hydrochloride, ephedrine hydrochloride, tetrahydrozoline hydrochloride, naphthazoline nitrate, oxymetazoline hydrochloride, xylometazoline hydrochloride and tramazoline hydrochloride, preferably oxymetazoline hydrochloride.

The pharmaceutical compositions can be complemented by various optional ingredients including one or more preservatives, sequestering agents, colouring agents and flavouring agents.

Suitable sequestering agents for incorporation herein include polycarboxylates, amino polycarboxylates, polyphosphates, polyphosphonates and aminopolyphosphonates such as ethylenediaminetetra-acetic acid (EDTA), diethylenetriaminepenta-acetic acid, citric acid, gluconic acid, pyrophosphoric acid, etc. as well as their water-soluble salts, especially the alkali metal, ammonium and alkanol ammonium salts. Sequestering agents are generally employed in amounts in the range from about 0.001 % to about 0.2 %, preferably from about 0.01 % to about 0.1 % by weight of the final pharmaceutical composition.

The pharmaceutical compositions can additionally include preservatives. These can be water-soluble or solubilizable preservatives such as DMDM Hydantoin(RTM), Germall(RTM) 115, methyl, ethyl, propyl, and butyl esters of hydrobenzoic acid, benzoic acid, Euxyl(RTM) K400, Bronopol(RTM) (2-bromo-2-nitropropane-1,3-diol), sodium benzoate, chlorhexadine, benzalkonium chlorides and 2-phenoxyethanol, parabens, benzyl alcohols, chlorbutol, phenoxyethanol, Cetrimide, potassium sorbate and thiomersal. Preferred preservatives for inclusion in the present invention are methyl and propyl parabens. In general, amounts of from about 0.005 % to about 0.5 % are suitable herein with amounts of from about 0.01 % to about 0.1 % being preferred.

Suitable flavouring agents for use herein include aromatic flavouring agents such as menthol, camphor and eucalyptol.

In accordance with a second aspect of the invention a carboxyl-containing polymer is used in a topical sprayable nasal medicament composition for preventing or minimizing "roll-back". The carboxyl-containing polymer is present in an amount of from about 0.05 % to about 5 %, preferably from about 0.25 % to about 2.5 % by weight of composition and is prepared by polymerizing one or more carboxyl-containing monoethyleneically unsaturated monomers and from about 0.05 % to about 5 % by weight of the polymer of a crosslinking agent. The carboxyl-containing polymer is used in combination with a surfactant and a pharmaceutically-acceptable nasal medicament. The surfactant is preferably present in an amount of from 0 to about 1 %, preferably from 0.4 % to about 0.8 % by weight of composition. The surfactant is selected from anionic, cationic, amphoteric and zwitterionic surfactants, and mixtures thereof. Said use gives a composition with a pH in the range from about 2.5 to about 6 and is administrable in sprayable form. The viscosity of the composition increases upon contact with the nasal linings of the nasal cavity to form a viscous gel.

In preferred embodiments of the invention the compositions are preferably provided in the form of a preferably pump-actuated

aerosol spray. Compositions herein preferably have a viscosity in the range up to about 300,000 mPa.s, more preferably up to about 20,000 mPa.s under low shear conditions (measured using a Brookfield RVT Viscometer, Spindle 7, 1 rpm, 25°C) and a viscosity in the range up to about 10,000 mPa.s, more preferably up to about 5000 mPa.s under high shear conditions (measured using a Brookfield RVT Viscometer, Spindle 7, 100 rpm, 25°C). The compositions have a pH in the range from about 2.5 to about 6. The spray pump for use in the administering of unit dosages of pharmaceutical compositions of the present invention is preferably of a finger-actuated pump design. The compositions are applied intra-nasally in a unit dosage containing from about 5 μg to about 100 μg, preferably from about 10 μg to about 50 μg of oxymetazoline per unit dose. In the preferred spray pump device (Perfect Valois VP7) there are approximately 1 to 3 sprays per unit dose. At least 95 % by weight of the compositions typically consist of particles having a spray particle size in the range of from about 10 μm to about 400 μm.

"Roll-back" testing is carried out using a randomized cross-over design on a minimum base size of 32 people, pre-screened to exclude subjects having colds or taking medication. The dose volume is 100 μl and is dispensed using a metered dose pump. Each subject uses a product according to the invention and a polymer-free control product, the minimum time between usage of the products being 24 hours. Users are instructed to blow their nose, tilt the head back slightly and spray the product once through each nostril inhaling gently after spraying. The users are then asked to provide favourable/unfavourable comments on a number of in-use characteristics, including roll-back and drop-out from the nasal cavity. Comparison of the two sprays by the subjects shows that the product according to the invention is significantly better at eliminating "roll-back" and drip out from the nasal cavity than the polymer-free control product.

The present invention is illustrated by the following examples.

Examples

Topical nasal medicament compositions of the invention are prepared with the following ingredients:

Compound	I/%	II/%	III/%	IV/%
menthol	0.025	0.025	0.025	0.025
eucalyptol	0.0075	0.006	0.007	0.0065
Carbopol 974P[1]	1.0	0.5	0.65	0.75
oxymetazoline	0.05	0.05	0.06	0.05
EDTA/diNa salt	0.05	0.045	0.06	0.05
methyl parabens	0.065	0.065	0.065	0.065
propyl parabens	0.035	0.035	0.035	0.035
sodium lauryl sulphate	0.8	0.45	0	0.5
water	to 100	to 100	to 100	to 100
pH	3.2	5.0	4.1	4.4

1. Manufactured and supplied by B.F.Goodrich Chemical Company, U.S.A.

Hot pre-dissolution of methyl and/or propyl parabens in water is carried out at 70°C followed by addition of Carbopol (RTM) 974P via a sieve to effect thorough wetting of the Carbopol (RTM). The remaining ingredients are added to the mixture and the pH is adjusted.

The compositions are incorporated into Perfect Valois VP7 finger-actuated spray pump dispensers.

The pharmaceutical compositions of the above Examples provide a high availability of active ingredient while significantly reducing "roll-back".

WHAT IS CLAIMED IS:

1. A nasal spray product comprising a pump-actuated nasal dispenser equipped with a reservoir, spray head and liquid/air mixing means, wherein the reservoir contains a topical nasal medicament composition in the form of a sprayable liquid comprising:

i) from about 0.05 % to about 5 % by weight of composition of a carboxyl-containing polymer prepared by polymerizing one or more carboxyl-containing monoethyleneically unsaturated monomers and from about 0.1 % to about 5 % by weight of the polymer of a crosslinking agent,

ii) up to about 1 % by weight of composition of a surfactant selected from anionic, non-ionic, cationic, amphoteric and zwitterionic surfactants and mixtures thereof, and

iii) from about 0.005 % to about 5 % by weight of composition of a pharmaceutically-acceptable nasal medicament,

wherein said composition has a low shear viscosity (measured with a Brookfield RVT Viscometer, Spindle 7, 1 r.p.m., 25°C) of from about 0 to about 300,000 mPa.s, a high shear viscosity (measured with a Brookfield RVT Viscometer, Spindle 7, 100 r.p.m., 25°C) of from about 0 to about 10,000 mPa.s and a pH in the range of from about 2.5 to about 6 and wherein the composition is administrable to the nasal cavity in sprayable form, whereby upon contact with the nasal linings of the nasal cavity the viscosity of the composition increases so as to form a viscous gel.

2. A nasal spray product according to claim 1 wherein said cross-linking agent is selected from polyalkenyl polymer crosslinking agents containing two or more alkenyl ether groupings containing terminal $H_2C=C<$ groups prepared by etherifying a polyhydric

alcohol containing at least four carbon atoms and at least three hydroxyl groups with an alkenyl halide, and mixtures thereof.

3. A nasal spray product according to claim 2 wherein the crosslinking agent is selected from polyallyl sucrose and polyallylpentaerythritol, and mixtures thereof.

4. A nasal spray product according to claim 3 which comprises from about 0.25 % to 2.5 % by weight of the carboxyl-containing polymer.

5. A nasal spray product according to claim 4 wherein the surfactant is selected from anionic surfactants.

6. A nasal spray product according to claim 5 which comprises from about 0.4 % to about 0.8 % by weight of the surfactant.

7. A nasal spray product according to claim 6 wherein the nasal medicament is selected from anti-inflammatory agents, antihistamine agents, anticholinergics, anti-allergic agents and vasoconstrictors, and mixtures thereof.

8. A nasal spray product according to claim 7 wherein the nasal medicament is a vasoconstrictor.

9. A nasal spray product according to claim 8 wherein the vasoconstrictor is selected from oxymetazoline hydrochloride, xylometazoline hydrochloride, phenylephrine hydrochloride, ephedrine hydrochloride, tetrahydrozoline hydrochloride, naphthazoline nitrate and tramazoline hydrochloride and mixtures thereof.

10. A nasal spray product according to claim 9 wherein the vasoconstrictor is oxymetazoline.

11. A nasal spray product according to claim 10 wherein the composition has a low shear viscosity (measured with a Brookfield

RVT Viscometer, Spindle 7, 1 r.p.m., 25°C) of from about 0 to about 20,000 mPa.s and a high shear viscosity (measured with a Brookfield RVT Viscometer, Spindle 7, 100 r.p.m., 25°C) of from about 0 to about 5000 mPa.s.

12. A nasal spray product according to claim 11 wherein the composition has a pH in the range of from about 2.5 to about 6.

13. Use of from about 0.05 % to about 5 % by weight of composition of a carboxyl-containing polymer in a topical sprayable liquid nasal medicament composition for preventing or minimizing roll-back, wherein the carboxyl-containing polymer is prepared by polymerizing one or more carboxyl-containing monoethyleneically unsaturated monomers and from about 0.05 % to about 5 % by weight of the polymer of a crosslinking agent, and wherein the carboxyl-containing polymer is used in combination with from 0 to about 1 % by weight of composition of a surfactant selected from anionic, non-ionic, cationic, amphoteric and zwitterionic surfactants and mixtures thereof, and from about 0.005 % to about 5 % by weight of composition of a pharmaceutically-acceptable nasal medicament and wherein the composition has a pH in the range of from about 2.5 to about 6 and is administrable in sprayable form, whereby upon contact with the nasal linings of the nasal cavity the viscosity of the composition increases so as to form a viscous gel.